09/487,841

```
=> d his

     (FILE 'HOME' ENTERED AT 14:48:32 ON 28 FEB 2005)

     FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 14:49:36 ON 28 FEB
     2005
L1         43351 S DOWN?(3A)SYNDROME
L2           335 S (METHIONINE(3A)SYNTHASE(3A)REDUCTASE OR MTRR)(8A)(POLYMORPHIS
L3            36 S L1 AND L2
L4        324388 S CORONARY(4A)DISEASE
L5            32 S L2 AND L4
L6         15322 S NEURAL(W)TUBE(W)DEFECT
L7            69 S L2 AND L6
L8             4 S L7 AND LOW(5A)COBALAMIN
L9            18 DUP REM L3 (18 DUPLICATES REMOVED)
L10           21 DUP REM L5 (11 DUPLICATES REMOVED)
L11            1 DUP REM L8 (3 DUPLICATES REMOVED)

=> d au ti so 1-18 l9

L9   ANSWER 1 OF 18  CAPLUS  COPYRIGHT 2005 ACS on STN
AU   Olteanu, Horatiu; Wolthers, Kirsten R.; Munro, Andrew W.; Scrutton, Nigel
     S.; Banerjee, Ruma
TI   Kinetic and Thermodynamic Characterization of the Common Polymorphic
     Variants of Human Methionine Synthase Reductase
SO   Biochemistry (2004), 43(7), 1988-1997
     CODEN: BICHAW; ISSN: 0006-2960

L9   ANSWER 2 OF 18      MEDLINE on STN                    DUPLICATE 1
AU   Fillon-Emery Nathalie; Chango Abalo; Mircher Clotilde; Barbe Francoise;
     Blehaut Henri; Herbeth Bernard; Rosenblatt David S; Rethore Marie-Odile;
     Lambert Daniel; Nicolas Jean Pierre
TI   Homocysteine concentrations in adults with trisomy 21: effect of B
     vitamins and genetic polymorphisms.
SO   American journal of clinical nutrition, (2004 Dec) 80 (6) 1551-7.
     Journal code: 0376027. ISSN: 0002-9165.

L9   ANSWER 3 OF 18      MEDLINE on STN                    DUPLICATE 2
AU   Gueant Jean-Louis; Gueant-Rodriguez Rosa-Maria; Anello Guido; Bosco Paolo;
     Brunaud Laurent; Romano Corrado; Ferri Rafaele; Romano Antonino; Candito
     Mirande; Namour Bernard
TI   Genetic determinants of folate and vitamin B12 metabolism: a common
     pathway in neural tube defect and Down syndrome?.
SO   Clinical chemistry and laboratory medicine : CCLM / FESCC, (2003 Nov) 41
     (11) 1473-7.  Ref: 38
     Journal code: 9806306. ISSN: 1434-6621.

L9   ANSWER 4 OF 18  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
AU   Barkai, Gad [Reprint Author]; Arbuzova, Svetlana; Berkenstadt, Michal;
     Heifetz, Sigal; Cuckle, Howard
TI   Frequency of Down's syndrome and neural-tube defects
     in the same family.
SO   Lancet (North American Edition), (April 19 2003) Vol. 361, No. 9366, pp.
     1331-1335. print.
     ISSN: 0099-5355 (ISSN print).

L9   ANSWER 5 OF 18      MEDLINE on STN                    DUPLICATE 3
AU   Zijno A; Andreoli C; Leopardi P; Marcon F; Rossi S; Caiola S; Verdina A;
     Galati R; Cafolla A; Crebelli R
TI   Folate status, metabolic genotype, and biomarkers of genotoxicity in
     healthy subjects.
SO   Carcinogenesis, (2003 Jun) 24 (6) 1097-103.  Electronic Publication:
     2003-04-24.
```

Journal code: 8008055. ISSN: 0143-3334.

L9 ANSWER 6 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AU Thurmon, T. F. [Reprint Author]; Yanamandra, K. [Reprint Author]; Ursin, S. A. [Reprint Author]; Chen, H. [Reprint Author]; Bocchini, J. A. [Reprint Author]; Layton, K. M.
TI MTHFR C677T and **MTRR** A66G **polymorphisms** in the etiology of Orofacial clefts from west Africa.
SO Genetics in Medicine, (May-June 2003) Vol. 5, No. 3, pp. 225. print.
Meeting Info.: Annual Clinical Genetics Meeting. San Diego, CA, USA. March 13-16, 2003.
ISSN: 1098-3600 (ISSN print).

L9 ANSWER 7 OF 18 MEDLINE on STN DUPLICATE 4
AU Bosco Paolo; Gueant-Rodriguez Rosa-Maria; Anello Guido; Barone Concetta; Namour Fares; Caraci Filippo; Romano Antonino; Romano Corrado; Gueant Jean-Louis
TI Methionine synthase (MTR) 2756 (A --> G) **polymorphism**, double heterozygosity methionine **synthase** 2756 AG/**methionine synthase reductase** (MTRR) 66 AG, and elevated homocysteinemia are three risk factors for having a child with **Down syndrome**.
SO Am J Med Genet A, (2003 Sep 1) 121 (3) 219-24.
Journal code: 101235741. ISSN: 1552-4825.

L9 ANSWER 8 OF 18 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
AU Zhu H P; Wicker N J; Shaw G M; Lammer E J; Hendricks K; Suarez L; Canfield M; Finnell R H (Reprint)
TI Homocysteine remethylation enzyme polymorphisms and increased risks for neural tube defects
SO MOLECULAR GENETICS AND METABOLISM, (MAR 2003) Vol. 78, No. 3, pp. 216-221.
Publisher: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.
ISSN: 1096-7192.

L9 ANSWER 9 OF 18 MEDLINE on STN
AU Sheth Jayesh J; Sheth Frenny J
TI Gene polymorphism and folate metabolism: a maternal risk factor for **Down syndrome**.
SO Indian pediatrics, (2003 Feb) 40 (2) 115-23.
Journal code: 2985062R. ISSN: 0019-6061.

L9 ANSWER 10 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AU Ge, Y.; Jensen, T.; James, S. J.; Becton, D. L.; Massey, G. V.; Weinstein, H. J.; Ravindranath, Y.; Matherly, L. H.; Taub, J. W. [Reprint Author]
TI High frequency of the 844ins68 cystathionine-beta-synthase gene variant in **Down syndrome** children with acute myeloid leukemia.
SO Leukemia (Basingstoke), (November 2002) Vol. 16, No. 11, pp. 2339-2341. print.
ISSN: 0887-6924 (ISSN print).

L9 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AU Tamai, Hiroshi
TI Visual clinical nutrition 2001. Vitamin metabolic disorder
SO Rinsho Eiyo (2002), 101(6), 617-625
CODEN: RNEYAW; ISSN: 0485-1412

L9 ANSWER 12 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AU Ursin, S. A. [Reprint author]; Yanamandra, K. [Reprint author]; Gadi, I.; Chen, H. [Reprint author]; Thurmon, T. F. [Reprint author]; Napper, D.

[Reprint author]; Dhanireddy, R. [Reprint author]; Bocchini, J. A., Jr. [Reprint author]
TI Is **methionine synthase reductase** 66G mutant genotype a risk factor for chromosomal **defects**?.
SO American Journal of Human Genetics, (October, 2002) Vol. 71, No. 4 Supplement, pp. 377. print.
Meeting Info.: 52nd Annual Meeting of the American Society of Human Genetics. Baltimore, MD, USA. October 15-19, 2002. American Society of Human Genetics.
CODEN: AJHGAG. ISSN: 0002-9297.

L9 ANSWER 13 OF 18 MEDLINE on STN DUPLICATE 5
AU O'Leary Valerie B; Parle-McDermott Anne; Molloy Anne M; Kirke Peadar N; Johnson Zachary; Conley Mary; Scott John M; Mills James L
TI **MTRR** and MTHFR **polymorphism**: link to **Down syndrome**?.
SO American journal of medical genetics, (2002 Jan 15) 107 (2) 151-5.
Journal code: 7708900. ISSN: 0148-7299.

L9 ANSWER 14 OF 18 MEDLINE on STN DUPLICATE 6
AU Hassold T J; Burrage L C; Chan E R; Judis L M; Schwartz S; James S J; Jacobs P A; Thomas N S
TI Maternal folate polymorphisms and the etiology of human nondisjunction.
SO American journal of human genetics, (2001 Aug) 69 (2) 434-9. Electronic Publication: 2001-07-05.
Journal code: 0370475. ISSN: 0002-9297.

L9 ANSWER 15 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AU Petersen, M. B. [Reprint author]; Grigoriadou, M. [Reprint author]; Mikkelsen, M.
TI Polymorphisms in genes involved in folate metabolism are not maternal risk factors for **Down syndrome**.
SO American Journal of Human Genetics, (October, 2001) Vol. 69, No. 4 Supplement, pp. 323. print.
Meeting Info.: 51st Annual Meeting of the American Society of Human Genetics. San Diego, California, USA. October 12-16, 2001.
CODEN: AJHGAG. ISSN: 0002-9297.

L9 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
IN Gravel, Roy A.; Rozen, Rima; Leclerc, Daniel; Wilson, Aaron; Rosenblatt, David
TI Human methionine synthase reductase and cDNA and methods for evaluating risk of neural tube defects, cardiovascular disease, cancer, and **Down's syndrome**
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2

L9 ANSWER 17 OF 18 MEDLINE on STN DUPLICATE 7
AU Hobbs C A; Sherman S L; Yi P; Hopkins S E; Torfs C P; Hine R J; Pogribna M; Rozen R; James S J
TI Polymorphisms in genes involved in folate metabolism as maternal risk factors for **Down syndrome**.
SO American journal of human genetics, (2000 Sep) 67 (3) 623-30. Electronic Publication: 2000-08-07.
Journal code: 0370475. ISSN: 0002-9297.

L9 ANSWER 18 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 8
AU Yi, P. [Reprint author]; Hobbs, C.; Melnyk, S.; Sherman, S.; Gravel, R.; Wu, Q.; Rozen, R.; James, S. J.
TI **Polymorphisms** in the methylenetetrahydrofolate reductase (MTHFR) and in the **methionine synthase reductase**

(MTRR) genes increase maternal risk of **Down syndrome**.
SO FASEB Journal, (March 15, 2000) Vol. 14, No. 4, pp. A231. print.
Meeting Info.: Annual Meeting of Professional Research Scientists: Experimental Biology 2000. San Diego, California, USA. April 15-18, 2000. Federation of American Societies for Experimental Biology.
CODEN: FAJOEC. ISSN: 0892-6638.

=> d bib 16 19

L9 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:493687 CAPLUS
DN 133:115929
TI Human methionine synthase reductase and cDNA and methods for evaluating risk of neural tube defects, cardiovascular disease, cancer, and **Down's syndrome**
IN Gravel, Roy A.; Rozen, Rima; Leclerc, Daniel; Wilson, Aaron; Rosenblatt, David
PA McGill University, Can.
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000042196	A2	20000720	WO 2000-IB209	20000114
	WO 2000042196	A3	20010125		
	W: CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 2003082676	A1	20030501	US 1999-371347	19990810
	CA 2360555	AA	20000720	CA 2000-2360555	20000114
PRAI	US 1999-232028	A	19990115		
	US 1999-371347	A	19990810		
	US 1998-71622P	P	19980116		
	WO 2000-IB209	W	20000114		

=> d au ti so 1-21 l10

L10 ANSWER 1 OF 21 MEDLINE on STN DUPLICATE 1
AU Miriuka Santiago G; Langman Loralie J; Evrovski Jovan; Miner Steven E S; D'Mello Nisha; Delgado Diego H; Wong Betty Y L; Ross Heather J; Cole David E C
TI Genetic polymorphisms predisposing to hyperhomocysteinemia in cardiac transplant patients.
SO Transplant international : official journal of the European Society for Organ Transplantation, (2005 Jan) 18 (1) 29-35.
Journal code: 8908516. ISSN: 0934-0874.

L10 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
AU Olteanu, Horatiu; Wolthers, Kirsten R.; Munro, Andrew W.; Scrutton, Nigel S.; Banerjee, Ruma
TI Kinetic and Thermodynamic Characterization of the Common Polymorphic Variants of Human Methionine Synthase Reductase
SO Biochemistry (2004), 43(7), 1988-1997
CODEN: BICHAW; ISSN: 0006-2960

L10 ANSWER 3 OF 21 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
AU Brune N; Andrich J; Gencik M; Saft C; Muller T (Reprint); Valentin S; Przuntek H; Epplen J T

TI Methyltetrahydrofolate reductase polymorphism influences onset of Huntington's disease
SO JOURNAL OF NEURAL TRANSMISSION-SUPPLEMENT, (26 JUL 2004) No. 68, pp. 105-110.
Publisher: SPRINGER, 233 SPRING STREET, NEW YORK, NY 10013 USA.
ISSN: 0303-6995.

L10 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
AU Botto, Nicoletta; Andreassi, Maria Grazia; Manfredi, Samantha; Masetti, Serena; Cocci, Franca; Colombo, Maria Giovanna; Storti, Simona; Rizza, Antonio; Biagini, Andrea
TI Genetic polymorphisms in folate and homocysteine metabolism as risk factors for DNA damage
SO European Journal of Human Genetics (2003), 11(9), 671-678
CODEN: EJHGEU; ISSN: 1018-4813

L10 ANSWER 5 OF 21 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AU Ghaedi, M. [Reprint Author]; Aleyassin, A. [Reprint Author]; Davoodi, S.; Abbasi, H.
TI Genetic variation of methylen tetrahydrofolate reductase gene in Iranian patients with **coronary** artery **disease**.
SO American Journal of Human Genetics, (November 2003) Vol. 73, No. 5, pp. 450. print.
Meeting Info.: 53rd Annual Meeting of the American Society of Human Genetics. Los Angeles, CA, USA. November 04-08, 2003. American Society of Human Genetics.
CODEN: AJHGAG. ISSN: 0002-9297.

L10 ANSWER 6 OF 21 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
AU D'Angelo A (Reprint); Mazzola G; Fermo I
TI Gene-gene and gene-environment interactions in mild hyperhomocysteinemia
SO PATHOPHYSIOLOGY OF HAEMOSTASIS AND THROMBOSIS, (DEC 2003) Vol. 33, No. 5-6, Sp. iss. SI, pp. 337-341.
Publisher: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND.
ISSN: 1424-8832.

L10 ANSWER 7 OF 21 MEDLINE on STN DUPLICATE 2
AU Brilakis Emmanouil S; Berger Peter B; Ballman Karla V; Rozen Rima
TI Methylenetetrahydrofolate reductase (MTHFR) 677C>T and **methionine synthase reductase** (**MTRR**) 66A>G **polymorphisms**: association with serum homocysteine and angiographic **coronary** artery **disease** in the era of flour products fortified with folic acid.
SO Atherosclerosis, (2003 Jun) 168 (2) 315-22.
Journal code: 0242543. ISSN: 0021-9150.

L10 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
AU Jacques, Paul F.; Bostom, Andrew G.; Selhub, Jacob; Rich, Sharron; Curtis Ellison, R.; Eckfeldt, John H.; Gravel, Roy A.; Rozen, Rima
TI Effects of **polymorphisms** of **methionine synthase** and **methionine synthase reductase** on total plasma homocysteine in the NHLBI Family Heart Study
SO Atherosclerosis (Shannon, Ireland) (2003), 166(1), 49-55
CODEN: ATHSBL; ISSN: 0021-9150

L10 ANSWER 9 OF 21 MEDLINE on STN DUPLICATE 4
AU Ashavaid Tester F; Shalia Kavita K; Kondkar Altaf A; Todur Seema P; Nair Kappiareth G; Nair Sunita R
TI Gene polymorphism and coronary risk factors in Indian population.
SO Clinical chemistry and laboratory medicine : CCLM / FESCC, (2002 Oct) 40 (10) 975-85. Ref: 100

Journal code: 9806306. ISSN: 1434-6621.

L10 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5
AU Jang, Yangsoo; Park, Hyun Young; Lee, Jong Ho; Ryu, Ha Jung; Kim, Ji Young; Kim, Oh Yoen
TI A **polymorphism** of the methylenetetrahydrofolate **reductase** and **methionine synthase** gene in CAD patients: association with plasma folate, vitamin B12 and homocysteine
SO Nutrition Research (New York, NY, United States) (2002), 22(9), 965-976
CODEN: NTRSDC; ISSN: 0271-5317

L10 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
AU Kim, Oh Yoen; Jang, Yangsoo; Lee, Jong Ho
TI Methylenetetrahydrofolate reductase and methionine synthase gene association with homocysteine metabolism and **coronary** artery **disease**
SO Nutritional Sciences (2002), 5(4), 256-258
CODEN: NSUCC5; ISSN: 1229-232X

L10 ANSWER 12 OF 21 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
AU Anwar W; Gueant J L (Reprint); Abdelmouttaleb I; Adjalla C; Gerard P; Lemoel G; Erraess N; Moutabarrek A; Namour F
TI Hyperhomocysteinemia is related to residual glomerular filtration and folate, but not to methylenetetrahydrofolate-**reductase** and **methionine synthase polymorphisms**, in supplemented end-stage renal disease patients undergoing hemodialysis
SO CLINICAL CHEMISTRY AND LABORATORY MEDICINE, (AUG 2001) Vol. 39, No. 8, pp. 747-752.
Publisher: WALTER DE GRUYTER & CO, GENTHINER STRASSE 13, D-10785 BERLIN, GERMANY.
ISSN: 1434-6621.

L10 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
IN Gravel, Roy A.; Rozen, Rima; Leclerc, Daniel; Wilson, Aaron; Rosenblatt, David
TI Human methionine synthase reductase and cDNA and methods for evaluating risk of neural tube defects, cardiovascular disease, cancer, and Down's syndrome
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2

L10 ANSWER 14 OF 21 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
AU Rozen R (Reprint)
TI Genetic modulation of homocysteinemia
SO SEMINARS IN THROMBOSIS AND HEMOSTASIS, (SEP 2000) Vol. 26, No. 3, pp. 255-261.
Publisher: THIEME MEDICAL PUBL INC, 333 SEVENTH AVE, NEW YORK, NY 10001.
ISSN: 0094-6176.

L10 ANSWER 15 OF 21 MEDLINE on STN DUPLICATE 6
AU Brown C A; McKinney K Q; Kaufman J S; Gravel R A; Rozen R
TI A common **polymorphism** in **methionine synthase reductase** increases risk of premature **coronary** artery **disease**.
SO Journal of cardiovascular risk, (2000 Jun) 7 (3) 197-200.
Journal code: 9436980. ISSN: 1350-6277.

L10 ANSWER 16 OF 21 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
AU Brown C A (Reprint); McKinney K; Kaufman J S; Gravel R A; Rozen R
TI Association of gene **polymorphisms** in methylenetetrahydrofolate

reductase, **methionine synthase** and **methionine synthase reductase** with homocysteine levels and **coronary** artery **disease**
SO CIRCULATION, (2 NOV 1999) Vol. 100, No. 18, Supp. [S], pp. 3982-3982. Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621. ISSN: 0009-7322.

L10 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
AU Morita, Hiroyuki; Kurihara, Hiroki; Sugiyama, Takao; Hamada, Chikuma; Kurihara, Yukiko; Shindo, Takayuki; Oh-Hashi, Yoshio; Yazaki, Yoshio
TI Polymorphism of the methionine synthase gene: association with homocysteine metabolism and late-onset vascular diseases in the Japanese population
SO Arteriosclerosis, Thrombosis, and Vascular Biology (1999), 19(2), 298-302 CODEN: ATVBFA; ISSN: 1079-5642

L10 ANSWER 18 OF 21 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
AU Fodinger M (Reprint); Buchmayer H; SunderPlassmann G
TI Molecular genetics of homocysteine metabolism
SO MINERAL AND ELECTROLYTE METABOLISM, (JUL-DEC 1999) Vol. 25, No. 4-6, pp. 269-278. Publisher: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND. ISSN: 0378-0392.

L10 ANSWER 19 OF 21 MEDLINE on STN
AU Morita H; Kurihara H; Sugiyama T; Kitamura K; Suzuki S; Sumiyoshi T; Yazaki Y
TI Genetic **polymorphisms** of methylenetetrahydrofolate **reductase** and **methionine synthase**: association with homocysteine metabolism and late-onset vascular diseases in the Japanese population.
SO Journal of cardiology, (1999 Feb) 33 (2) 106-7. Journal code: 8804703. ISSN: 0914-5087.

L10 ANSWER 20 OF 21 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AU Brown, Charlotte A. [Reprint author]; McKinney, Kimberly Q. [Reprint author]; Kaufman, Jay S. [Reprint author]; Gravel, Roy A.; Rozen, Rima
TI Association of gene **polymorphisms** in methylenetetrahydrofolate **reductase**, **methionine synthase** and **methionine synthase reductase** with homocysteine levels and **coronary** artery **disease**.
SO Circulation, (Nov. 2, 1999) Vol. 100, No. 18 SUPPL., pp. I.754. print. Meeting Info.: 72nd Scientific Sessions of the American Heart Association. Atlanta, Georgia, USA. November 7-10, 1999. CODEN: CIRCAZ. ISSN: 0009-7322.

L10 ANSWER 21 OF 21 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AU Adjalla, C.; Abdel Mouttaleb, I.; Gastin, I.; Angioi, M.; Gueant, J. L.; Danchin, N.
TI Methylene tetrahydrofolate **reductase** and **methionine synthase polymorphisms** are not associated with angiographically-documented **coronary** artery **disease**.
SO European Heart Journal, (Aug., 1998) Vol. 19, No. ABST. SUPPL., pp. 346. print.
Meeting Info.: XXth Congress of the European Society of Cardiology. Vienna, Austria. August 22-26, 1998. European Society of Cardiology.
CODEN: EHJODF. ISSN: 0195-668X.

=> d bib l11

L11 ANSWER 1 OF 1 MEDLINE on STN DUPLICATE 1
AN 1999375459 MEDLINE
DN PubMed ID: 10444342
TI A common variant in methionine synthase reductase combined with **low cobalamin** (vitamin B12) increases risk for spina bifida.
AU Wilson A; Platt R; Wu Q; Leclerc D; Christensen B; Yang H; Gravel R A; Rozen R
CS The Montreal Children's Hospital Research Institute, McGill University, Montreal, Quebec, Canada.
NC HL58955-01 (NHLBI)
SO Molecular genetics and metabolism, (1999 Aug) 67 (4) 317-23. Journal code: 9805456. ISSN: 1096-7192.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199909
ED Entered STN: 19991005
Last Updated on STN: 19991005
Entered Medline: 19990922

=> d ab l11

L11 ANSWER 1 OF 1 MEDLINE on STN DUPLICATE 1
AB Impairment of folate and cobalamin (vitamin B(12)) metabolism has been observed in families with **neural tube defects** (NTDs). Genetic variants of enzymes in the homocysteine remethylation pathway might act as predisposing factors contributing to NTD risk. The first polymorphism linked to increased NTD risk was the 677C-->T mutation in methylenetetrahydrofolate reductase (MTHFR). We now report a **polymorphism** in **methionine synthase reductase** (**MTRR**), the enzyme that activates cobalamin-dependent methionine synthase. This polymorphorism, 66A-->G (I22M), has an allele frequency of 0.51 and increases NTD risk when **cobalamin** status is **low** or when the MTHFR mutant genotype is present. Genotypes and cobalamin status were assessed in 56 patients with spina bifida, 58 mothers of patients, 97 control children, and 89 mothers of controls. Cases and case mothers were almost twice as likely to possess the homozygous mutant genotype when compared to controls, but this difference was not statistically significant. However, when combined with **low** levels of **cobalamin**, the risk for mothers increased nearly five times (odds ratio (OR) = 4.8, 95% CI 1.5-15.8); the OR for children with this combination was 2.5 (95% CI 0.63-9.7). In the presence of combined MTHFR and MTRR homozygous mutant genotypes, children and mothers had a fourfold and threefold increase in risk, respectively (OR = 4.1, 95% CI 1.0-16.4; and OR = 2.9, 95% CI 0.58-14.8). This study provides the first genetic link between vitamin B(12) deficiency and NTDs and supports the multifactorial origins of these common birth defects. Investigation of this polymorphism in other disorders associated with altered homocysteine metabolism, such as vascular disease, is clearly warranted.

=>